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09/893,348	06/28/2001	Michal Eisenbach-Schwartz	EIS-SCHWARTZ=2A	1155

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/893,348	Applicant(s) EISENBACH-SCHWARTZ ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *3-30,33-37,40 and 42-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,31,32,38,39 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-44* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/314,161*.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group IX, claims 1-6, 31-40, 41-43, drawn to a method for preventing or inhibiting neuronal degeneration comprising administering a peptide derived from an NS-specific antigen in Paper No. 10 (04 November 2002) is acknowledged. The traversal is on the ground(s) that the six techniques of Groups I-VI and VII-XII are all techniques for obtaining the same result (is, generating NS-specific activated T cells). Applicant argues that this can be done by administering the T cells themselves, or by administering an antigen or a peptide, or a nucleotide sequence that causes the expression of such an antigen or peptide, in order to activate T cells thereagainst *in vivo*. Applicant also asserts that claim 1 is effectively a Markush-type claim and that it is improper for the Office to refuse to examine that which applicants regard as their invention unless the subject matter in the claim lack unity of invention. Applicant contends that unity of invention is present because all of the embodiments share the same technical feature (i.e., causing the production of NS-specific activated T cells). Applicant submits that the invention is the same whether used to promote nerve regeneration or to inhibit neuronal degeneration since the present invention causes either or both to occur depending on the injury or disease being treated. Applicant argues that the ingredients, process steps, and endpoints are the same regardless of whether regeneration is being promoted or degeneration is being inhibited. This is not found persuasive. As discussed in the previous Office Action (Paper No. 9, 02 October 2002), Inventions I-XII are different methods because they require different ingredients, process steps, and endpoints. For example, Invention I requires search and consideration of efficacy of therapy of T cell administration to promote nerve regeneration while

Invention VIII requires search and consideration of efficacy of therapy of NS-specific antigen administration to prevent or inhibit neuronal degeneration. Although NS-specific activated T cells may eventually be generated in the inventions of Groups I-XII, each invention requires the administration of a different product to an individual and each invention has a different outcome—either nerve regeneration or prevention/inhibition of neuronal degeneration. Each of Groups I-XII is a unique invention, requiring a unique search of the prior art. Searching all of the inventions in a single patent application would provide an undue search burden on the examiner and the USPTO's resources because of the non-coextensive nature of these scarches.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-30, 33-37, 40, and 42-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10 (04 November 2002).

Claims 1-2, 31-32, 38-39, and 41 are under consideration in the instant application as they read upon the elected species of injury, central nervous system, spinal cord injury, Nogo-A, and subcutaneously.

Information Disclosure Statement

It is noted to Applicant that two citations (Wekerle and Hirschberg et al.) have been crossed out by the Examiner because these citations were referenced on an earlier page in the same PTO-1449 (Paper No. 6, 28 June 2001).

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specification

2. The disclosure is objected to because of the following informalities:

3. Patent applications are referenced in the disclosure (pg 5, lines 17-18; pg 58, line 11). The status of the applications must be updated.

4. The Brief Description of Drawings at pg 22 does not refer to Figures 18A and 18B.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "A METHOD FOR PROMOTING RECOVERY FROM SPINAL CORD INJURY BY ADMINISTERING A PEPTIDE DERIVED FROM A NS-SPECIFIC ANTIGEN".

Appropriate correction is required.

Claim Objections

6. Claims 1-2, 31, and 41 are objected to because of the following informalities: Claims 1-2, 31 and 41 recite non-elected groups and species.

Appropriate correction is required.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 31-32, and 41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 6-7, and 16 of copending Application No. 09/218,277. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims in the '277 application and the instant application recite a method of administering to an individual in need thereof an effective amount of an ingredient selected from the group consisting of NS-specific T cells, a NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen. The recitation of preventing or inhibiting neuronal degeneration to ameliorate the effects of injury or disease in the preamble of the claims from the '277 application and the instant application is interpreted as an intended use and bears no accorded patentable weight. Regarding both applications, the administration of the same recited agents to an individual, particularly a peptide derived from an NS-specific antigen, will elicit the same response in the body, regardless of the phrasing of the preamble. The claims in the instant application encompass the limitations recited

in the '277 application. Therefore, the instant claims of a method of administering to an individual in need thereof an effective amount of an ingredient selected from the group consisting of NS-specific T cells, a NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen is not patentably distinct over the co-pending claims in Application No. 09/218,277.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2, 31-32, 38-39, and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for promoting recovery from spinal cord injury comprising subcutaneously administering to an individual in need thereof a composition comprising a peptide derived from Nogo-A, as set forth in SEQ ID NO: 19, and wherein said composition promotes recovery from spinal cord injury, does not reasonably provide enablement for a method for preventing or inhibiting neuronal degeneration in the central nervous system for ameliorating the effects of injury, comprising administering to an individual in need thereof a peptide derived from an NS-specific antigen or from an analog thereof, or an analog or derivative of said peptide. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method for preventing or inhibiting neuronal degeneration in the central nervous system for ameliorating the effects of injury, comprising administering to an individual in need thereof a peptide derived from an NS-specific antigen or from an analog thereof, or an analog or derivative of said peptide. The claims also recite that the injury is a spinal cord injury and that the peptide derived from an NS-specific antigen is an immunogenic epitope or a cryptic epitope derived from Nogo. The claims recite that the peptide is the Nogo-A p472 peptide of SEQ ID NO: 19 and that the NS-specific antigen or peptide derived therefrom is administered subcutaneously.

The specification teaches that pre-immunized (p472) SPD male and female rats are subjected to severe spinal cord contusion and a 10-g rod is dropped onto the laminectomized cord (pg 93, lines 19-23). The specification discloses that the rats are immunized subcutaneously with Nogo p472 peptide emulsified in CFA containing *Mycobacterium tuberculosis* while control rats are injected with PBS emulsified in CFA (pg 93, line 24 through pg 94, lines 1-14). The specification teaches that hind limb motor skills of the animals are scored since a therapeutic approach aiming at reducing the spread of damage through neuroprotection will result in better recovery in terms of hind limb motor activity (pg 94, lines 21-24 through pg 95, line 1). Furthermore, the specification teaches that male and female p472-immunized rats significantly improve in overall functional recovery compared to control rats (pg 95, lines 5-17; Figures 24A-B, Figure 25). However, the specification does not teach preventing neuronal degeneration in the central nervous system of any individual by administering a peptide derived from an NS-

specific antigen. The term "preventing" is interpreted as meaning that an activity will not occur, i.e. neuronal degeneration will not occur. Undue experimentation would be required of the skilled artisan to determine the quantity of NS-specific antigen (Nogo) to be administered, the best route of administration, the duration of treatment, and any possible side-effects to completely prevent neuronal degeneration.

Furthermore, there are no methods or working examples in the specification that indicate the administration of a Nogo-derived peptide to injured rats specifically inhibits neuronal degeneration. The examples at pg 94-95 of the specification teach the measurement of hind limb locomotion in p472-immunized and control rats. However, the specification does not indicate a nexus between hind limb locomotion performance and neuronal degeneration. For example, there are no methods in the specification teaching one skilled in the art to measure (on average) the quantity of viable neurons or axon sprouting before and after the spinal cord injury. There is also no guidance indicating that a certain number of viable neurons or axon sprouting is associated with a certain level of locomotor activity and that this activity is an indication of inhibition of or no inhibition of neuronal degeneration. The administration of the p472 Nogo peptide may affect other physiological mechanisms other than primary neuronal degeneration, such as secondary neuronal degeneration or interference with the binding of other proteins/receptors.

Additionally, the specification does not disclose that all possible peptides derived from Nogo-A promote functional recovery from spinal cord contusion or able to prevent or inhibit neuronal degeneration in the central nervous system of an individual. A large quantity of experimentation would be required by the skilled artisan to administer all possible Nogo-A-

derived peptides and monitor their effects in rats. The Examiner has interpreted the administration of Nogo-A p472 (SEQ ID NO: 19) to be a critical feature of the claimed method since relevant literature teaches that other Nogo-A derived peptides possess growth-cone-collapsing activity and inhibit neurite outgrowth (for example, GrandPre et al. Nature 403: 439-444, 2000; see pg 442, Figures 4-5).

The specification also does not teach that all possible peptides derived from all possible NS-specific antigens are able to prevent or inhibit neuronal degeneration in the central nervous system of an individual. Undue experimentation would be required of the skilled artisan to generate peptides to all possible NS-specific antigens and administer each of these peptides to an individual to achieve the desired result of preventing or inhibiting neuronal degeneration. Since the specification also provides no guidance regarding what type of analogs of the NS-specific antigen and analogs and derivatives of the peptide should be utilized for the desired activity, the skilled artisan must resort to trial and error experimentation to determine which class of compounds might yield one with the desired activity. Such trial and error experimentation is considered undue. According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis".

Due to the large quantity of experimentation necessary to prevent neuronal degeneration in an individual, to determine a nexus between administration of a peptide derived from a NS-specific antigen and neuronal degeneration, and to generate peptides to all possible NS-specific

antigens and administer each of these peptides to an individual, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the unpredictability of the effects of the administration of all possible peptides derived from NS-specific antigens in an individual, and the breadth of the claims which fail to recite any structural limitations about a specific peptide derived from an NS-specific antigen, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-2, 31-32, 38-39, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Regarding claims 1-2, 31-32, 38-39, and 41, the acronym "NS" renders the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

12. The term "from an analog thereof" in claims 1-2, 31-32, 38-39, and 41 is a relative term which renders the claim indefinite. The term "from an analog thereof" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined what compounds or proteins are encompassed by this terminology. For example, antibodies, similar peptides, binding proteins, etc.?

13. Regarding claim 2, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

14. Claims 1-2, 31-32, 38-39, and 41 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that administration of a peptide derived from an NS-specific antigen prevents or inhibits neuronal degeneration.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Brittis P et al. Neuron 30(1): 11-14, 2001.

Brosamle et al. J Neurosci 20(21): 8061-8068, 2000.

Chen et al. Nature 403 : 434-439, 2000.

GrandPre et al. Nature 403 : 439-444, 2000.

GrandPre et al. Nature 417 : 547-551, 2002.

Hauben et al. Proc Natl Acad Sci USA 98(26) : 15173-15178, 2001.

Huber A et al. J. Neurosci 22(9): 3553-3567, 2002.

Merkler et al. J. Neurosci 21(10): 3665-3673, 2001.

Prinjha et al. Nature 403 : 383-384, 2000.

Wickelgren, I. Science 297 : 178-181, 2002.

Woolf et al. Science 297 : 1132-1134, 2002.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
January 24, 2003

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600